CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Withdrawn-Presently Presented) A liquid pharmaceutical formulation for the prolonged release of interleukin(s), this formulation comprising an aqueous colloidal suspension of low viscosity based on submicronic particles of water - soluble biodegradable polymer (PO) carrying hydrophobic groups (HG), said particles being non - covalently associated with at least one active principle (AP),

wherein at least one of the at least one active principle(s) is an interleukin,

wherein the dispersion medium of said aqueous colloidal suspension consists essentially of water,

wherein said formulation is capable of being injected parenterally and forming a gelled deposit *in vivo*,

wherein the formation of a gelled deposit is at least partly caused by at least one physiological protein present *in vivo*, and makes it possible to prolong and control the *in vivo* release time of the AP beyond 24 h after administration,

wherein said formulation is liquid under the injection conditions, and does not form a gelled deposit at the physiological temperature and/or physiological pH-and/or in the presence of: a physiological electrolyte in a physiological concentration, and/or at least one surfactant .

2. (Withdrawn-Previously Presented) The formulation according to claim 1, characterized in that its concentration of PO is set at a sufficiently high value to allow the

formation of a gelled deposit *in vivo* after parenteral injection, in the presence of at least one physiological protein.

3. (Previously Presented) A liquid pharmaceutical formulation for the prolonged release of at least one active principle(s) (AP),

wherein at least one of the at least one active principle(s) is an interleukin,

wherein said formulation is liquid in the ambient atmosphere and is liquid at physiological temperatures, at physiological pH, in the presence of a physiological electrolyte in a physiological concentration, or in the presence of at least one surfactant,

and wherein said formulation comprises an aqueous colloidal suspension of low viscosity comprising submicronic particles of water - soluble biodegradable polymer PO carrying hydrophobic groups HG, wherein said submicronic particles are non - covalently associated with at least one active principle AP, and wherein the dispersion medium of the aqueous colloidal suspension of low viscosity consists consisting essentially of water, and

wherein the concentration of PO is sufficiently high such that a gelled deposit forms *in vitro* in an aqueous solution comprising bovine serum albumin in a concentration of 30 mg/ml.

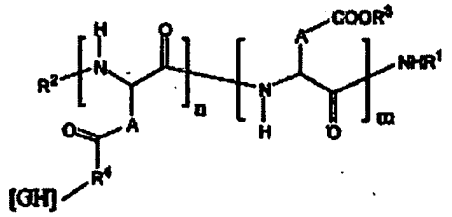
4. (Previously Presented) The formulation according to claim 3, wherein the concentration of PO is greater than or equal to 0.9 C1 where C1 is the "induced gelling" concentration of the particles of PO, as measured in an IG test.

5. (Previously Presented) The formulation according to claim 3, wherein the viscosity of the aqueous colloidal suspension is less than or equal to 5 Pa.s at 25°C.

6. (Previously Presented) The formulation according to claim 3, wherein the polymer PO is a polyamino acid comprising aspartic units, glutamic units, or both aspartic and

glutamic units, wherein at least one of said unit carries at least one graft comprising at least one hydrophobic group (HG).

7. (Previously Presented) The formulation according to claim 6, wherein the PO is defined by general formula (I) below:



(I)

wherein:

R^1 is selected from the group consisting of: H, a linear C2 to C10 alkyl, a branched C3 to C10 alkyl, a benzyl, a terminal amino acid unit, and $-R^4-[HG]$;

R^2 is selected from the group consisting of: H, a linear C2 to C10 acyl, a branched C3 to C10 acyl group, a pyroglutamate, and $-R^4-[HG]$;

R^3 is H or a cationic entity selected from the group consisting of: sodium metal cations, potassium metal cations, calcium metal cations, magnesium metal cations, organic cations based on amine, organic cations based on oligoamine, organic cations based on polyamine, polyethylenimine, organic cations based on amino acid(s), organic cations based on lysine, organic cations based on arginine, cationic polyamino acids comprising polylysine and, cationic polyamino acids comprising oligolysine;

R^4 is a direct bond or a spacer based on 1 to 4 amino acid units;

A independently is a radical $-CH_2-$ (aspartic unit) or $-CH_2-CH_2-$ (glutamic unit);

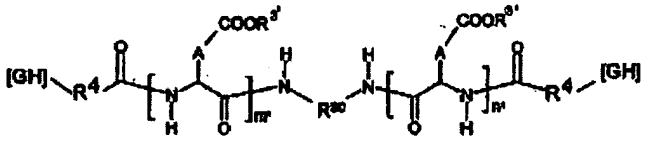
n/(n + m) is defined as the molar grafting rate and varies from 0.5 to 100 mol%;

n + m varies from 10 to 1000; and

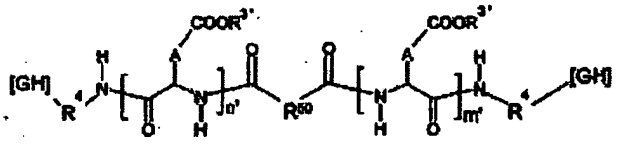
HG is a hydrophobic group.

8. (Previously Presented) The formulation according to claim 6, wherein the PO has one of general formulae (II), (III) and (IV) below:

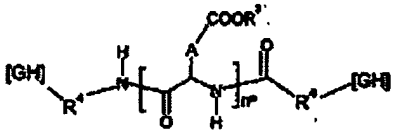
(II)



(III)



(IV)



wherein:

HG is a hydrophobic group;

R^{30} is a linear C2 to C6 alkyl group;

$R^{3'}$ is selected from the group consisting of: H, sodium metal cations, potassium metal cations, calcium metal cations, magnesium metal cations, organic cations based on amine, organic cations based on oligoamine, organic cations based on polyamine, organic cations based on amino acid(s), organic cations based on lysine, organic cations based on arginine, cationic polyamino acids comprising polylysine, and cationic polyamino acids comprising oligolysine;

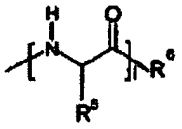
R^{50} is a C2 to C6 alkyl, dialkoxy, or diamine group;

R^4 is a direct bond or a spacer based on 1 to 4 amino acid units;

A independently is a radical - CH_2 - (aspartic unit) or - CH_2 - CH_2 - (glutamic unit); and

n' + m' or n" is defined as the degree of polymerization and varies from 10 to 1000.

9. (Previously Presented) The formulation according to claim 7, wherein each HG of the PO each independently of one another is a monovalent radical having the formula below:



(HG)

wherein:

R^5 is selected from the group consisting of: a methyl group (alanine), an isopropyl group (valine), an isobutyl group (leucine), a sec - butyl group (isoleucine), and a benzyl group (phenylalanine);

R^6 is a hydrophobic radical containing from 6 to 30 carbon atoms;

l varies from 0 to 6.

10. (Previously Presented) The formulation according to claim 9, wherein at least one hydrophobic radical R^6 of the PO is independently selected from the group of radicals consisting of:

a linear or branched alkoxy group containing from 6 to 30 carbon atoms;

a linear or branched alkoxy group containing (i) from 6 to 30 carbon atoms and (ii) at least one heteroatom, at least one unit of unsaturation, or both at least one heteroatom and at least one unit of unsaturation;

an alkoxy group containing 6 to 30 carbon atoms and having one or more fused carbocyclic ring,

an alkoxy group containing 6 to 30 carbon atoms, having one or more fused carbocyclic rings, and containing at least one unit of unsaturation, at least one heteroatom, or both at least one heteroatom and at least one unit of unsaturation;

an alkoxyaryl group or an aryloxyalkyl group having 7 to 30 carbon atoms; and

an alkoxyaryl group or an aryloxyalkyl group having 7 to 30 carbon atoms and containing at least one unit of unsaturation, at least one heteroatom, or both at least one heteroatom and at least one unit of unsaturation.

11. (Previously Presented) The formulation according to claim 9 or claim 10, wherein the hydrophobic radical R^6 is derived from an alcohol precursor selected from the group consisting of octanol, dodecanol, tetradecanol, hexadecanol, octadecanol, oleyl alcohol, tocopherol, and cholesterol.

12. (Previously Presented) The formulation according to claim 6, wherein the PO consists of an alpha - L - glutamate or alpha - L - glutamic homopolymer.

13. (Previously Presented) The formulation according to claim 6, wherein the PO consists of an alpha - L - aspartate or alpha - L - aspartic homopolymer.

14. (Previously Presented) The formulation according to claim 6, wherein the PO consists of an alpha - L - aspartate/alpha - L - glutamate or alpha - L - aspartic/alpha - L - glutamic copolymer.

15. (Previously Presented) The formulation according to claim 14, wherein the PO comprises a distribution of aspartic units carrying at least one HG unit, glutamic units carrying at least one HG unit, or both aspartic units carrying at least one HG unit and glutamic units

carrying at least one HG unit is such that the resulting polymer is random, of the block type, or of the multiblock type.

16. (Withdrawn-Previously Presented) The formulation according to claim 1, characterized in that the molecular weight of the PO is between 2000 and 100,000 g/mol.

17. (Previously Presented) The formulation according to claim 7, wherein the hydrophobic radical R^6 is derived from tocopherol, and wherein

$1\% \leq [n/(n+m)] \times 100 \leq 10\%$, and

$n + m$ varies from 100 to 400.

18. (Previously Presented) The formulation according to claim 7, wherein the hydrophobic radical R^6 is derived from cholesterol:

$1\% \leq [n/(n+m)] \times 100 \leq 10\%$, and

$n + m$ varies from 100 to 400.

19. (Previously Presented) The formulation according to claim 7 wherein the concentration of polymer PO is between 15 and 50 mg/ml.

20. (Previously Presented) The formulation according to claim 3, wherein the viscosity of the aqueous colloidal suspension is less than or equal to 5 Pa.s at 25°C.

21. (Previously Presented) The formulation according to claim 3, wherein the polymer PO is selected from the group consisting of: polyamino acids, polysaccharides, pullulans, chitosans, mucopolysaccharides, gelatins, and mixtures thereof.

22. (Previously Presented) The formulation according to claim 3, wherein the % weight fraction of interleukin(s) not associated with the submicronic particles ≤ 1.

23. (Previously Presented) The formulation according to claim 3, wherein the interleukin is interleukin 2.

24. (Previously Presented) The formulation according to claim 3, further comprising at least one active principle(s) selected from the group consisting of a protein, a glycoprotein, a protein bonded to one or more polyalkylene glycol chains, polyethylene glycol (PEG) chains, a polysaccharide, a liposaccharide, an oligonucleotide, a polynucleotide, a peptide, haemoglobins, cytochromes, albumins, interferons, cytokines, antigens, antibodies, erythropoietin, insulin, growth hormones, factors VIII and IX, haemopoiesis stimulating factors, and mixtures thereof.

25. (Previously Presented) The formulation according to claim 3, wherein said formulation is injectable by the parenteral route, by the subcutaneous route, by the intramuscular route, by the intradermal route, by the intraperitoneal route, by the intracerebral route, or into a tumour.

26. (Previously Presented) The formulation according to claim 3, wherein said formulation is intended for the preparation of drugs administered by the parenteral route, by the subcutaneous route, by the intramuscular route, by the intradermal route, by the intraperitoneal route, by the intracerebral route by the oral route, by the nasal route, by the vaginal route, by the ocular route, or into a tumour,.

27. (Withdrawn-Previously Presented) A process for the preparation of drugs, particularly for administration by the parenteral, subcutaneous, intramuscular, intradermal, intraperitoneal or intracerebral route or into a tumour, or by the oral, nasal, vaginal or ocular route, characterized in that it consists essentially in using at least one formulation according to claim 3.

28. (Withdrawn-Previously Presented) A derived product, comprising submicronic particles formed of non - covalent PO/AP associations as defined in claim 1.

29. (Withdrawn-Previously Presented) The derived product according to claim 28, wherein said formulation comprises a powder or a gel.

30. (Withdrawn-Previously Presented) A method for the preparation of the formulation according to claim 3, said method comprising the steps of:

preparing a colloidal suspension of nanoparticles comprising at least one PO,

mixing said colloidal suspension of nanoparticles comprising at least one PO with at least one interleukin and at least one additional active principle(s) (AP) in aqueous solution,

adding at least one excipient,

adjusting the pH, the osmolarity , or both, and

filtering the resulting suspension.

31. (Withdrawn-Previously Presented) The method according to claim 30, characterized in that the at least one additional AP is in the form of an aqueous suspension or solution.

32. (Withdrawn-Previously Presented) A method for the preparation of the formulation according to claim 3, said method comprising the steps of:

making a powder comprising at least one polymer PO,

mixing said powder with an aqueous suspension or solution comprising at least one interleukin and at least one additional active principle(s) in aqueous solution,

adding at least one excipient,

adjusting the pH, the osmolarity, or both, and

filtering the resulting suspension.

33. (Withdrawn-Previously Presented) A method for the preparation of a pharmaceutical formulation said method comprising the steps of drying the liquid formulation according to claim 3 to produce a powder,

mixing said powder with an aqueous liquid medium

adding at least one excipient,

adjusting the pH, the osmolarity, or both, and

filtering the resulting suspension.

34. (Withdrawn-Previously Presented) A method for the preparation of a powder pharmaceutical formulation said method comprising the step of drying the formulation according to claim 3.

35. (Previously Presented) The formulation according to claim 3, wherein the concentration of PO is greater than or equal to C1 and is less than or equal to 20.C1, where C1 is the "induced gelling" concentration of the particles of PO, as measured in an IG test.

36. (Previously Presented) The formulation according to claim 3, wherein the concentration of PO is greater than or equal to C1 and is less than or equal to 10.C1, where C1 is the "induced gelling" concentration of the particles of PO, as measured in an IG test.

37. (Previously Presented) The formulation according to claim 7, wherein the molar grafting rate is sufficiently low for PO, dissolved in water at pH 7 and at 25°C, to form a colloidal suspension of submicronic particles of PO.

38. (Previously Presented) The formulation according to claim 7, wherein $n/(n + m)$ is being between 1 and 25 mol%.

39. (Previously Presented) The formulation according to claim 7, wherein $n/(n + m)$ is being between 1 and 15 mol%.

40. (Previously Presented) The formulation according to claim 7, wherein n + m is between 50 and 300.